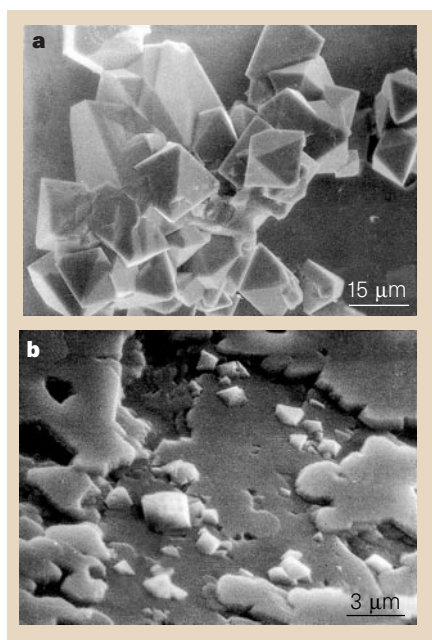


(Fig. 1a) but  $\text{Na}_2\text{CO}_3\text{--C}$  diamond nucleation was not established under similar conditions. At a temperature as low as 1,150 °C for 120 hours, there was spontaneous nucleation of diamond octahedra of up to 4  $\mu\text{m}$  and growth on seeds.

In the  $\text{K}_2\text{CO}_3\text{--C}$  system, diamonds grew on the seed crystals between 1,300 and 1,420 °C, but there was no nucleation. For the  $\text{K}_2\text{CO}_3 + \text{C--O--H fluid} + \text{C}$  system, after 20 and 40 hours at 1,250–1,420 °C, we also observed growth on seeds but without nucleation. However, runs of 120 hours at 1,150 °C, in the case of  $\text{Na}_2\text{CO}_3$  with fluid as well, led to spontaneous diamond nucleation and growth on seeds (Fig. 1b). In all experiments in which fluid was added, we found metastable graphite in the form of small crystals. X-ray diffraction analysis did not reveal any decomposition of carbonates.

Diamond nucleation in the alkaline carbonate–graphite and alkaline carbonate–fluid–graphite systems, at the pressure and temperature studied, is largely determined by kinetics and takes place only in runs lasting tens of hours. The period of induction preceding diamond nucleation and growth increases as the temperature is decreased. This is the main difference between diamond synthesis in carbonate and metal melts.

Taking into account the influence of kinetics on diamond-forming processes, the established nucleation and growth temperature of 1,150 °C can hardly be supposed to be minimal, as it is lower than in the metal–graphite systems<sup>6</sup>. Catalytic activity in the system decreases in the sequence  $\text{Na}_2\text{CO}_3 + \text{C--O--H fluid} + \text{C} > \text{K}_2\text{CO}_3 + \text{C--O--H fluid} + \text{C} > \text{Na}_2\text{CO}_3\text{--C} > \text{K}_2\text{CO}_3\text{--C}$ . Diamond growth rates vary in the range 0.01–4  $\mu\text{m h}^{-1}$ , depending on the



**Figure 1** Scanning electron micrographs of diamonds. **a**, Octahedral diamonds (run NF-2). **b**, Diamond growth layers and spontaneous diamonds on {111} face of seed crystal (run KF-3).

temperature and composition of the crystallization medium. In the ‘dry’ melt of  $\text{Na}_2\text{CO}_3$ , diamond crystallizes in the form of cubo-octahedra, and octahedra are formed in alkaline carbonate fluid–melts, which are most typical for natural diamonds.

Alkaline carbonate–fluid melts approximate the composition of a diamond-producing mantle environment<sup>7–9</sup>. Considering the abundance of carbonates in diamond-bearing rocks of magmatic<sup>1</sup> and metamorphic<sup>10</sup> origin, as well as the aqueous carbonaceous composition of mantle fluid<sup>7</sup>,

we suggest that alkaline carbonate–fluid melts represent the most likely medium for natural diamond formation.

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## Ageing, fitness and neurocognitive function

In the ageing process, neural areas<sup>1,2</sup> and cognitive processes<sup>3,4</sup> do not degrade uniformly. Executive control processes and the prefrontal and frontal brain regions that support them show large and disproportionate changes with age. Studies of adult animals indicate that metabolic<sup>5</sup> and neurochemical<sup>6</sup> functions improve with aerobic fitness. We therefore investigated whether greater aerobic fitness in adults would result in selective improvements in executive control processes, such as planning, scheduling, inhibition and working memory. Over a period of six months, we studied 124 previously sedentary adults, 60 to 75 years old, who were randomly assigned to either aerobic (walking) or anaerobic (stretching and toning) exercise. We found that those who received aerobic training showed substantial improvements in performance on tasks requiring executive control compared with anaerobically trained subjects.

Each of the 124 subjects was given a cardiorespiratory fitness test, in which the rate of oxygen consumption was measured, and a variety of cognitive tasks, including task switching<sup>7</sup>, response compatibility<sup>8</sup> and stopping<sup>9</sup>. These tasks were chosen because a subset of their conditions require executive control processes and they have been shown through human lesion, neuroimaging and animal studies to be supported by frontal or prefrontal regions of the brain.

Task switching is a measure of the ‘cost’ of switching between tasks, indicated by the difference in reaction time between those trials in which subjects switch between tasks and those in which they continue to perform the same task; response compatibility

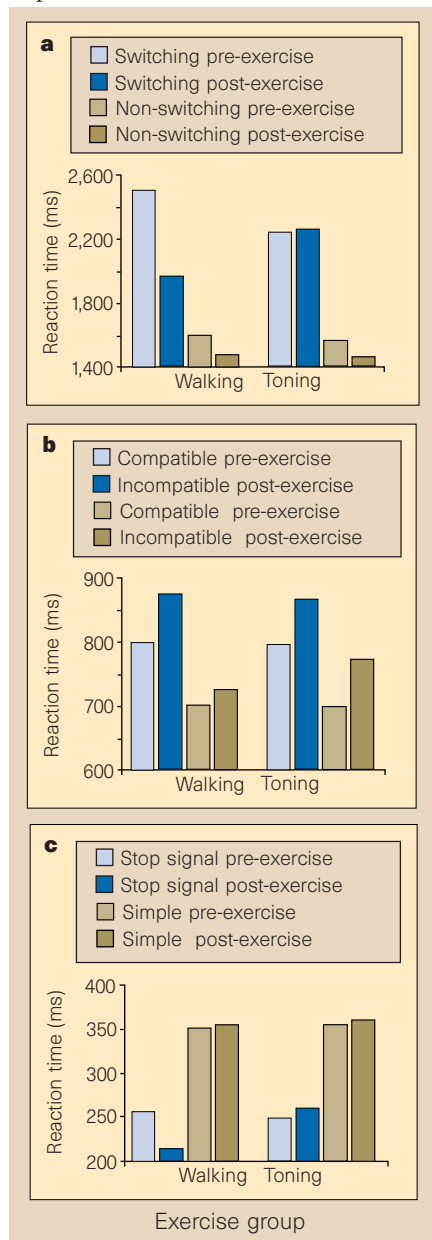
**Table 1 Experimental results at 5.7 GPa**

Number	Temperature (°C)	Time (h)	Nucleation of diamond	Growth on seeds	Thickness of diamond layer ( $\mu\text{m}$ )	
					{100} face	{111} face
<b><math>\text{Na}_2\text{CO}_3 + \text{graphite}</math></b>						
N-1	1,420	20	No	Yes	4	3
N-2	1,420	30	S (5 $\mu\text{m}$ )	Yes	18	20
N-3	1,420	40	S (40 $\mu\text{m}$ )	Yes	40	35
N-3	1,360	40	No	Yes	20	6
N-5	1,360	40	No	Yes	12	10
N-6	1,360	40	No	No	–	–
<b><math>\text{K}_2\text{CO}_3 + \text{graphite}</math></b>						
K-1	1,420	30	No	Yes	10	1
K-2	1,420	40	No	Yes	15	3
K-3	1,300	40	No	Yes	8	2
K-4	1,250	40	No	No	–	–
<b><math>\text{Na}_2\text{CO}_3 + \text{H}_2\text{C}_2\text{O}_4 \cdot 2\text{H}_2\text{O} + \text{graphite}</math></b>						
NF-1	1,420	20	S (13 $\mu\text{m}$ )	Yes	20	14
NF-2	1,360	40	S (65 $\mu\text{m}$ )	Yes	60	45
NF-3	1,250	40	No	Yes	10	8
NF-4	1,150	120	S (4 $\mu\text{m}$ )	Yes	3	1.5
<b><math>\text{K}_2\text{CO}_3 + \text{H}_2\text{C}_2\text{O}_4 \cdot 2\text{H}_2\text{O} + \text{graphite}</math></b>						
KF-1	1,420	20	No	Yes	~1	~1
KF-2	1,250	40	No	Yes	25	4
KF-3	1,150	120	S (2 $\mu\text{m}$ )	Yes	1.5	1

S, spontaneous nucleation; the size of newly crystallized diamonds is shown in parentheses.

is a measure of the ability to ignore task-irrelevant stimuli, indicated by the difference between reaction time on response-compatible and response-incompatible trials; and stopping is a measure of the ability to abort a preprogrammed action, indicated by the reaction time to stop an action after a 'stop signal'.

Performance in other conditions on these same tasks, such as reaction time in the non-switch trials in the task-switching test, in the compatible trials on the response-compatibility task, and simple reaction time in the stopping test, depend less on executive control processes and so would not be expected to benefit from improvements in aerobic fitness.



**Figure 1** Tasks predicted to show selective improvements in performance for the walking but not for the toning group. **a**, Task switching; **b**, response compatibility; **c**, stopping. Experimental details are available from the authors.

Subjects in the walking group showed a significant improvement in the maximum rate of oxygen consumption (5.1%) compared with the toning group (−2.8%) after exercise training; the two groups displayed equivalent scores before exercise training.

Consistent with our 'selective improvement' hypothesis, performance improved significantly for subjects in the aerobic but not the toning group for task conditions depending on executive control processes (Fig. 1). In the task-switching test, subjects in the walking but not the toning group became much faster at switching between tasks following fitness training. Performance on the non-switch trials was equivalent for the walking and toning groups. In the response-compatibility test, the distractor-interference effect (difference between incompatible and compatible reaction times) decreased for the aerobic but not for the toning group, but there was no difference between groups on the compatible trials. In the stopping test, the reaction time for stopping was reduced for the aerobic but not for the toning subjects, whereas simple reaction time was the same for the two groups.

The three measures that were dependent on executive control processes and the integrity of the prefrontal and frontal cortex were all sensitive to the exercise intervention. However, the beneficial effect of aerobic exercise was selective: it did not affect performance on other measures in the same tasks that were not tied to frontally mediated executive functions.

The selective nature of the improvements produced by aerobic exercise, which affect only executive control processes supported by frontal and prefrontal regions of the brain, might explain the ambiguity of previous studies<sup>10</sup> relating aerobic fitness with improved neurocognitive function. The improvement we find requires only small increases in aerobic fitness.

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## Developmental model for thalidomide action

Tabin has proposed a progress-zone model<sup>1</sup>, based on published data, to explain the inhibition of limb morphogenesis by thalidomide. We do not think that his model convincingly explains the main features of thalidomide action.

We have previously listed<sup>2</sup> the factors that must be taken into account to explain the teratogenic action of thalidomide. First, the mechanism must be shown to occur in the embryo (preferably in a primate). Second, it must take into account the species specificity of thalidomide: it is teratogenic in all primates tested, has little effect in rabbits, and is not teratogenic in mice and rats. Third, thalidomide induces malformation of several organs but not of others, such as the brain. The heart, too, is an important target, and the many early postnatal deaths were probably due to cardiac malformation.

Any hypothesis on the teratogenicity of thalidomide should also be able to explain the defects induced in other organs by a common mechanism, which we believe cannot be inhibition of proliferation. It must also explain the sensitive period of thalidomide's action, which is confined to about two weeks in primates, although many induction and proliferation processes occur before and after this period. It needs to account for abnormal development but should not be too general because thalidomide has high specificity. The pattern of typical abnormalities cannot be mimicked by any other known teratogen, so its action must be unusual. Furthermore, thalidomide has many effects in different systems and dose levels, and few of these will be relevant to its teratogenic action.

With regard to Tabin's hypothesis<sup>1</sup>, we must consider the fact that the critical period for thalidomide-induced typical limb malformations (amelia and phocomelia) is very early. According to investigations in primates<sup>3,4</sup>, developmental stages 11 to 14 are affected, reaching (for example in the marmoset *Callithrix jacchus*) a maximum<sup>5,6</sup> at stages 11 to 12. Upper limb buds start to develop as early as stage 11. The apical ectodermal ridge (AER), which is critical according to Tabin's hypothesis, does not occur until stage 14, too late to bring about amelia or phocomelia.

We prefer an alternative explanation of